UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D C 20231
www uspto gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,550	06/18/2001	William E. Marshall	P01936US5	1897

22885 7590 12/17/2002

MCKEE, VOORHEES & SEASE, P.L.C.
801 GRAND AVENUE
SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	6

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/883,550	MARSHALL, WILLIAM E.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

The instant application is a continuation of U.S. Patent Application 09/193,653 filed on 11-17-1998. Reference to said application is missing.

Election/Restrictions

Applicant's election of Group I in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-22 are pending. Claims 20-22 have been withdrawn from consideration as being drawn to non-elected inventions. Claims 1-19 are currently under examination.

Applicant's preliminary amendment (Paper No. 3) is acknowledged. Said amendment contained arguments and a 1.132 declaration addressing rejections made in the parent case. Applicant is reminded that each application is examined based on its own merits. Since there are no rejections of record with regard to the instant application, said arguments are premature and will not be addressed herein.

Claim Objections

Claim 12 is objected to because of the following informalities: the abbreviation SRF is used without defining its meaning when initially used. Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the phrase "activating and modulating". It is unclear what immunological functions the term "modulating" encompasses. Additionally, is activation not considered a form of modulation? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 1 is rendered vague and indefinite by the use of the phrase "filtering said separated product to remove any stress response products having a molecular weight greater than 10 kDa". It is unclear what Applicant is claiming. Is the claimed filtering process removing only stress response products with a molecular weight greater than 10 kDa or all substances with a molecular weight greater than 10 kDa? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 8 is rendered vague and indefinite by the use of the phrase "37 C **or less**". Since there is no lower limit set forth in the claim it is impossible to know what temperature the

claimed invention becomes non-functional. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Claim 10 is rendered vague and indefinite by the use of the term "stationary phase". It is unclear whether Applicant is referring to a stage of replication or motility. As such, it is impossible to determine the metes and bounds of the claimed invention.

Claim 11 is rendered vague and indefinite by the use of the phrase "molecular weight cutoff of 10,000. Since there are no units associated with the number 10,000 it is impossible to determine the metes and bounds of the claimed invention.

Claim 12 recites the limitation ""the method of claim 1 wherein the filtrate containing SRFs <10lDa..."" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 15 is rendered vague and indefinite by the use of the phrase "having a size of between 0.5 and 3 kDa". Kilodaltons are units of measure used for the molecular weight of a molecule not its size.

Claims 17-19 are rendered vague and indefinite by the use of the phrase "sequential periods of stress". It is unclear what is meant by said phrase. Does the stress factor change with each successive "period"? Are there rest periods (i.e. removal of stress factors) in between these "periods"? If not, what demarcates the end of one period and the onset of the next? As written, it is impossible to determine the metes and bounds of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 5,840,318. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are all drawn to methods of activating and modulating the immune systems of animals b the administration of stress response factors released by stressed bacteria.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 and 17-19 are drawn to methods of modulating the immune system of an animal through the administration of the supernatant from stressed bacterial cultures to the animal. Said bacteria are stressed by reducing the bioavailability of nutrients through the placement of said bacteria in a nun-nutritive solution. Claims 1, 11, 12 and 15 require the

removal of proteins larger than 10 kDa and are being examined as a method of modulating the immune system of an animal by administering a low molecular weight fraction of the supernatant from a stressed bacterial culture.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being obvious over Marshall et al. (U.S. Patent 5,840,318).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2). Marshall et al. disclose methods of activating and modulating the immune system of animals by the administration of stress response factors released by stressed bacteria (see

abstract and column 5, line 66 to column 10, line 44). The methods disclosed by Marshall et al., differ from the instant claims with regard to the pH of the PBS, incubation temperature of the bacteria and the specific types of filters used in purifying the SRPs. However, since the stress products (and their sources) disclosed by Marshall et al. are identical to those of the instant claims, the two methodologies merely constitute obvious minor variants of each other.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al. (Microbiology, Vol. 142, 1996, pages 817-827).

De Vuyst et al. disclose methods of producing low molecular weight proteins from bacteria by subjecting them to a number of stresses. These stresses include: a change in temperature, a change in pH, a change in biomass (crowding or decreasing the amount of media), and adding toxins such as ethanol (see abstract). Subjecting the lactic acid bacteria to any of these stressors results in the release of low molecular weight monomers of bacteriocin (approx 6 kDa or less) that oligomerize to be about 30 kDa. De Vuyst et al. remove components larger than the bacteriocin monomer (see page 818, column 1). De Vuyst et al. further disclose that these bacteriocins are able to kill or harm other bacterial species and suggests the use of said bacteriocins as food additives (see page 818, column 1). Consequently, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have followed the suggestion of De Vuyst et al. and administer the low molecular weight proteins produced by stressed bacteria to animals since said proteins (bacteriocins) can act to kill or render harmless other strains of bacteria and thereby enhancing the ability of an animal's immune system to deal

with bacterial infections minimizing the complications associated with introducing a bacterial strain into the normal flora of an animal..

Claims 1-15 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al., cited above, in view of Nanji (U.S. Patent 5,413,785 – IDS-2).

As outlined above, De Vuyst et al. disclose methods for producing low molecular weight proteins from stressed bacteria (bacteriocins) and suggests adding said proteins to food. Nanji discloses the administration of lactic acid bacteria to humans, livestock and other animals for protection against endotoxin-mediated shock. Nanji further discloses that said bacteria should be able to produce anti-microbial substances and/or produce proteinaceous antagonistic substances (bacteriocins) since said substances aid in preventing the growth of gram-positive and gram-negative bacteria in the intestine and thereby reducing endotoxin formation (see column 10, lines 40-45). Reduction of endotoxin levels, in turn, reduces the effects of said endotoxin on the immune processes of the animal. Therefore, it would have been obvious to one of ordinary skill in the art to use the bacteriocins disclosed by De Vuyst et al. in the treatment methodologies of Nanji in order to take advantage of the immune enhancing effects of the bacteriocins while minimizing the complications associated with introducing a bacterial strain into the normal flora of an animal. One would have had a high expectation of success since De Vuyst et al. disclose the use of said bacteriocins as a food additive and Nunji disclose the importance of bacteriocins in reducing endotoxin levels and thereby reducing the deleterious effects of said endotoxin on the animal's immune system.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over De Vuyst et al., cited above, in view of Perdigon et al. (Journal of Food Protection Vol. 53, No. 5, pages 404-410, 1996 – IDS-2) or Emery et al. (U.S. Patent 5,538,733).

Claim 16 is being examined as a method of modulating the immune system of an animal by administering low molecular weight stress proteins as an adjuvant. The teachings of De Vuyst et al. are discussed above. Perdigon et al. disclose the use of lactic acid bacteria and the proteins produced therein as adjuvants in the generation of protection from enteropathogens (see abstract, page 404, column 2 and pages 408-409). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the low molecular weight proteins disclosed by De Vuyst et al. as adjuvants for the induction of a immune response to another co-administered pathogen since Perdigon et al. discusses the use of lactic acid bacteria as adjuvants for enteropathogens (an increased immune response to said enteropathogens was also disclosed) and De Vuyst et al. disclose that proteins produced by lactic acid bacteria have an immunomodulatory effect.

Emery et al. disclose the use of a bacteriocin, such as the one disclosed by De Vuyst et al., in combination with a wide variety of pathogens (attenuated, killed or subunits thereof). Emery et al. further discloses that bacteriocin is an effective immunogen, as the administration of bacteriocin results in a good immune response that can prevent reinfection (see column 6, lines 5-36 and Example 2). Consequently, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the low molecular weight proteins (bacteriocins) disclosed by De Vuyst et al. in combination with another pathogen (i.e. as an

adjuvant) in order to take advantage of the active immune response that would be generated as set forth in Emery et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 608-7991. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Robert A Zeman
December 16, 2002